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Announcement

Allergy Abstracts has been published since 1936 by members of the Allergy Division of The Jewish Hospital of Brooklyn. The Editorial Board is comprised of former residents of this department who contribute their services.

Allergy Abstracts selects and abstracts those articles in the literature which may be of clinical or theoretical interest to workers in the field of allergy. Each abstract represents a summary of the author's findings and views, and its inclusion in Allergy Abstracts does not imply approval of its contents by the editor.—*The Editors.*

Asthma and Hay Fever

Intermittent Positive Pressure Breathing. Its Use in the Inspiratory Phase of Respiration. Segal, M. S., Salomon, A., Dulfano, M. J., and Herschfus, J. A.: New England J. Med. **250**: 225, 1954.

Intermittent positive pressure breathing in the inspiratory phase (IPPB/I) employing the Bennett valve (model TV-2P) was used in the treatment of 203 patients with pulmonary disease. The Bennett apparatus was arranged with an attachment for a plastic Vaponephrin nebulizer fed by separate low oxygen flow. Either air or oxygen was used in the treatments with or without bronchodilator solutions, such as Neosuprelz, Isuprel, or Vaponephrin in the nebulizer. Pressures of from 5 to 20 cm. of water were employed. In patients with superimposed bronchiolar infection, a suitable antibiotic was added to the aerosol solution and Pancreatic Dornase was administered to patients with viscous sputum. Treatments of twenty minutes' duration were given from one to three times a day for from five to six days. Patients with chronic pulmonary emphysema or bronchiectasis were advised to return monthly for two to four days of intensive treatment. Results were evaluated clinically according to the patient's subjective feeling, chest examinations, changes in cough and expectoration, and exercise tolerance. The vital capacity, maximal breathing capacity, and timed vital capacity were measured. Of fifty-three patients with bronchial asthma, three patients were slightly improved, twenty-eight experienced good results, and twenty-two were relieved of all symptoms. Among forty-four patients with chronic pulmonary emphysema, two patients were unimproved, six showed slight improvement, twenty-nine showed good results, and seven showed excellent results. Among eight patients with bronchiectasis, results were good in four and excellent in four. The treatment also was employed with good results in patients with pulmonary edema from irritating gases, cardiac failure, or in respiratory depression from drugs. Vital capacity studies indicated 20 per cent improvement following IPPB/I with bronchodilator aerosols, as compared to 10 per cent with bronchodilators only. Despite the clinical improvement noted with IPPB/I alone in patients with asthma, pulmonary emphysema, and bronchiectasis, the results indicated that this treatment caused a decrease of the maximal breathing capacity in 60 per cent of the determinations and of the timed vital capacity in 80 per cent. In addition, there was a decrease of the already low ratio of first-second to total vital capacity: from 52 per cent to 39 per cent after IPPB/I. The combination treatment (IPPB/I with bronchodilator drugs) improved the maximal breathing capacity 45.7 per cent over the controls in asthma, 35.5 per cent in chronic pulmonary emphysema, and 25 per cent in bronchiectasis. The first-second of the timed vital capacity was increased 18 per cent after the combined treatment and the total vital capacity was increased 17 per cent. In long-term treatment in which patients with pulmonary emphysema were given daily treatments of IPPB/I with bronchodilators up to sixty days, the average values for vital capacity were no better for the last five days of treatment than for the first five days. E. W.

Prantal, Orally, in the Treatment of Asthma and Nasal Allergies. A Preliminary Report. Frank, D. E., and MacLaren, W. R.: Ann. Allergy **12**: 289, 1954.

The anticholinergic drugs, such as Prantal, which are used in the treatment of peptic ulcer, exert their beneficial effects by producing "medical vagotomy." Thirty-eight allergic individuals and two patients with neurodermatitis were treated orally with Prantal. All the patients tolerated a

dosage of 100 mg. four times daily for about one month without ill effects. Contrary to the expected results, beneficial effects were not observed in the asthmatic patients, but persons suffering from vasomotor rhinitis and hay fever experienced considerable relief, particularly from rhinorrhea and sneezing. F.

Further Observations on Smoker's Respiratory Syndrome. Waldbott, G. L.: Ann. Int. Med. **39**: 1026, 1953.

Smoker's respiratory syndrome, or smoker's asthma, is characterized by chronic pharyngitis, wheezing, dyspnea on exertion, cough and expectoration, and a tendency to respiratory infections. Chest pains may occur, which are darting and angina-like in character. Of fifty-eight patients studied, thirty-four recovered completely upon cessation of smoking; the other twenty-four, who had copious purulent sputum, recovered upon cessation of smoking combined with antibiotic treatment. In addition, eight patients were observed who manifested irreversible changes and who previously had been diagnosed as "intrinsic" asthma or chronic emphysema. These patients obtained only temporary relief from elimination of smoking. There was presumptive evidence that the clinical findings in these patients represented the end result of smoker's syndrome. The secondary complicating changes were considered to be due to frequent upper respiratory infections. Skin reactions to tobacco were generally negative. The author concludes that allergy to tobacco played no part in smoker's respiratory syndrome and that the symptoms in these patients were due to "clinical irritation and subsequent inflammation from . . . irritants . . . present in tobacco smoke." J. S.

Dermatology

Local Use of Hydrocortisone Acetate: A Preliminary Report. Robinson, R. C. V.: Bull. Johns Hopkins Hosp. **93**: 147, 1953.

Hydrocortisone acetate ointment was used locally in 42 patients with atopic dermatitis, pruritus vulvae, pruritus ani, or discoid lupus erythematosus, who failed to improve on one or more other forms of local therapy.

Of 28 patients with atopic dermatitis, 20 obtained dramatic relief within twenty-four hours. Twelve of the 28 patients also showed objective improvement of involved areas distant from the site of application of the ointment. This suggested percutaneous absorption of the drug. Five of 8 patients with pruritus vulvae and one of 3 patients with pruritus ani responded favorably. Exacerbations occurred in all patients on cessation treatment. Significant improvement occurred in 3 patients with discoid lupus erythematosus.

Three patients complained of burning and itching in the areas where the ointment had been applied. Two of these patients gave positive patch reactions to the lanolin contained in the ointment base. J. S.

Studies of Sweating. VI. On the Urticariogenic Properties of Human Sweat. Sulzberger, M. B., Herrmann, F., Borota, A., and Strauss, M. B.: J. Invest. Dermat. **21**: 293, 1953.

Normal and atopic subjects were exposed to dry heat and specimens of their sweat were collected. The specimens were sterilized by pasteurization and then injected in 0.02 ml. amounts intracutaneously into the donor and other subjects. Reactions were read at from twenty to thirty minutes.

Autoinjections of sweat produced whealing in almost all subjects, but the reactions were much more pronounced in atopic subjects than in normals,

The sweat collected from normal donors after the inhalation or ingestion of various allergens tended to be more urticariogenic for atopic individuals than specimens collected prior to the exposures. Although it could not be proved that sweat collected after a donor's exposure to an allergen by inhalation or ingestion contained that allergen, nevertheless such sweat appeared to be slightly more urticariogenic in atopic individuals who were skin-sensitive to that allergen than in atopics who were not.

It was suggested that obstruction of sweat ducts may lead to diffusion of sweat into the tissues and by virtue of its urticariogenic properties may cause, maintain, or aggravate various pruritic, urticarial, and other irritative dermatoses. M. C.

The Case of a New Anticholinergic Agent, Piperphenamine, for the Control of Hyperhidrosis and Associated Dermatoses. Lubowe, I. I.: New York State J. Med. **53**: 2847, 1953.

A new anticholinergic compound known as piperphenamine (5-methyl-4-phenyl-[piperidyl]-3-hexanol methobromide) was used in the treatment of 40 cases of hyperhidrosis, miliaria, neurodermatitis, and other dermatoses associated with dysfunction of the sweat mechanism. Nine of 12 patients with hyperhidrosis of the palms and soles had noticeable suppression of perspiration. Six patients with occupational contact dermatitis who also had hyperhidrosis of the palms and soles responded well to treatment with piperphenamine. Five cases of neurodermatitis, with involvement of the antecubital spaces that were treated orally with the drug, cleared more rapidly than did 3 similar cases of neurodermatitis which were treated locally. Three cases of vasomotor rhinitis failed to show any improvement after one month of therapy. In all cases, the dose given varied from 150 to 200 mg. per day. Side effects were negligible. C.

Experimental Contact Dermatitis. I. Dinitrochlorobenzene Contact Dermatitis In Guinea Pigs. Zeligman, I.: J. Invest. Dermat. **22**: 109, 1954.

Dinitrochlorobenzene (DNCB) is a chemical which has frequently been employed to study contact dermatitis in laboratory animals. In this series of experiments DNCB was applied to the skin of guinea pigs in order to determine whether this chemical, in the concentrations and vehicle in which it is usually employed is an effective contact allergen. It was found that in the concentrations of 5 per cent in acetone, 1 per cent in acetone, and 0.1 per cent in petrolatum, DNCB could act as a primary irritant to the skin of guinea pigs. Because of its irritating properties, it was difficult to evaluate the sensitizing capacity of DNCB. It was not possible to differentiate histologically between the dermatitis induced by a primarily irritating concentration of DNCB in an unsensitized pig and that caused by an apparently specific response in the sensitized guinea pig. M. C.

Occupational Dermatitis in Government Workers. Becker, S. W., Jr.: J. Invest. Dermat. **22**: 249, 1954.

Allergic dermatoses constituted 34 per cent of the occupational dermatoses which occurred in 260 government workers during the course of one year. The most common causes of allergic contact dermatitis were the chemicals used in the printing and allied fields. Of these, chromate was the principal offender. Nonchromate ink was also an important sensitizer. Other chemicals which produced contact dermatitis included rubber, developing chemicals,

plastics, carbon paper, penicillin, and glue. There was one case of physical allergy attributed to photosensitization from digitalis seed and there were 22 cases of poison ivy. Primary irritants caused 43 per cent of the dermatoses, which was a lower percentage than was found in other industrial surveys.
M. C.

A Case of Allergic Cutaneous Vasculitis (Arteriolitis Allergica). Ruiter, M.: Brit. J. Dermat. **65**: 77, 1953.

The author has attempted to group together a number of skin disorders which have heretofore been unsatisfactorily defined under the heading of allergic cutaneous vasculitis. Although these diseases have different clinical manifestations and morphologic features, they are grouped together histopathologically on the basis of the presence of allergic inflammation of the cutaneous vessels (arteriolitis allergica). In contradistinction to periarteritis nodosa where the characteristic lesion is found in the medium-sized vessels at the level of the cutaneous-subcutaneous border, the inflammatory process in Arteriolitis Allergica is found in the smaller vessels of the corium. In several cases previously described, a positive personal or family history of allergy was obtained. Many of these cases were regarded as allergic bacterial dissemination reactions of the skin. Focal infection was demonstrated in some cases with lasting recovery obtained in one chronic case following the removal of such a focus. The author cites the case of a 51-year-old woman who developed papular and macular lesions which were primarily limited to the extremities. Some of these lesions had hemorrhagic crusts, others were surmounted by small vesicles. The physical examinations and laboratory findings were negative except for the presence of a right maxillary sinusitis. Smears showed gram-negative rods which could not be cultured. Histologic studies of a macule revealed inflammatory changes in the small vessels (mainly arterioles) of the corium with dissociation of the endothelial cells, and swelling and fibrinoid changes of the vessel walls, as well as fragmentation of the collagen and infiltration with polynuclear leukocytes and eosinophils. The affected vessels and their perivascular inflammatory infiltration formed a conglomeration of foci which extended over the stratum papillare and subpapillare.
E. W.

Kaposi's Varicelliform Eruption: Direct Transmission to a Nurse. Simpson, J. R.: Brit. J. Dermat. **65**: 139, 1953.

Two cases of Kaposi's varicelliform eruption due to the virus of herpes simplex are reported. The first patient, an 11-month-old boy who was hospitalized with infantile eczema probably acquired the eruption from a cold sore on his mother's lips. The course in this case was stormy and septic. The second patient was a 27-year-old nurse who cared for the infant and developed her initial lesion on an area of chapped skin on her hand. The virus of herpes simplex was isolated in each case.
E. W.

Urticaria and Angioedema in Children and Young Adults. Etiologic and Electrocardiographic Findings in One Hundred Fifteen Cases. Siegel, S. C., and Bergeron, J. G.: Ann. Allergy **12**: 241, 1954.

One hundred fifteen children and young adults with urticaria and angioedema were investigated in an effort to determine the etiological agents involved. Twenty-eight per cent of the group had a positive family history and 18 per cent had a personal history of allergy. Penicillin was found to be the

causative agent in twenty-eight cases (24 per cent). In the penicillin reactors, only 8 per cent had a personal history of allergy and 19 per cent a positive family history. Skin tests performed on nineteen of the penicillin cases yielded only five positive reactions by the scratch method and none by the intracutaneous route. There were fourteen patients (12 per cent) in whom foods were established as the precipitating agent. In twelve cases (10 per cent), infection was believed to be the causative factor. The case histories of these patients are presented to demonstrate the causal relationship between infection and the symptoms. In thirty-six patients (31 per cent), thorough investigation failed to establish the etiological factor. Electrocardiograms were performed on ninety-eight of the patients in the series. No changes attributable to the urticaria or angioedema were observed in any of the records.

H. F.

The Control of Tromexan Therapy. Olwin, J. H., and Friedman, I. A.: Surg., Gynec. & Obst. **99**: 22, 1954.

Tromexan, an anticoagulant, was administered to 135 patients. Of these, 128 were being treated for thromboembolic disease and seven suffered from other illnesses and acted as controls. The effects, results, and complications of and itching while on maintenance therapy. Some of these also had urticaria. Following withdrawal of the drug and administration of antihistaminics, the therapy are discussed. Eight patients developed a dermatitis with erythema skin complications cleared. Allergic studies were not reported. J. S.

Hydrocortisone Ointments: Their Rational Use in Dermatology. Welsh, A. L., and Ede, M.: Ohio M. J. **50**: 837, 1954.

Although hydrocortisone exerts the most potent anti-inflammatory action of any known steroid at tissue levels, its effect is usually of a temporary nature. Exacerbation frequently follows cessation of treatment and the eruptions then are often more difficult to control than originally.

Four hundred two patients with chronic dermatoses, mostly of an eczematous nature which were refractory to conventional topical therapy, were treated first with hydrocortisone ointment alone and later with hydrocortisone in combination with various other antieczematous topical medications. After improvement occurred, the hydrocortisone was gradually reduced in dosage application and then withdrawn entirely. In 235 patients, improvement was more rapid following treatment with the combined medications than with the antieczematous agents alone. Twenty-one patients who could not tolerate the antieczematous agents showed complete tolerance and excellent clinical response when the combined therapy was used.

In this series, it was apparent that hydrocortisone-free alcohol ointment was more effective and more rapid in controlling symptoms than hydrocortisone acetate ointment. There were three patients in this series who developed reactions to the topical hydrocortisone. Patch tests proved these reactions to be due to the base, rather than to the hydrocortisone itself. F.

Etiology of Nummular Eczema. Fowle, L. P., and Rice, J. W.: Arch. Dermat. & Syph. **68**: 69, 1953.

The authors studied 178 patients who were suffering from nummular eczema of the hands and compared them statistically with patients having other types of dermatitis of the hands. Females slightly outnumbered males in the group investigated. Most of the patients were in the third decade of life but all ages were represented. Nutrition, allergy, and infection were

investigated as possible etiological factors in nummular eczema. Patients with nummular eczema, as a class, tended to eat small quantities of meat and vegetables but large amounts of carbohydrates and fat. Signs of vitamin B deficiency were much more obvious in patients with nummular eczema than in patients with other types of eczematous eruptions of the venenata type. There was also a tendency to anemia, usually of the macrocytic type, in about one-third of the nummular eczema patients.

The incidence of atopic diseases was about the same among patients with nummular eczema and among patients with contact dermatitis. The incidence of tonsil infection, as well as styes, furuncles, circinary impetigo, and osteomyelitis, was significantly greater in patients with nummular eczema than in other groups. Cultures were made on routine blood agar plates of the nummular plaques from thirty-seven patients. Twenty-seven of these cultures showed *Staphylococcus aureus,* eight nonhemolytic staphylococci, four nonhemolytic streptococci, and six beta-hemolytic streptococci. In another study, a special mannitol salt agar plate was used for culturing the *Staphylococcus aureus.* Plates were pressed against the eczematoid lesions as well as against the normal skin of patients suffering from nummular eczema. The skin on various areas of normal persons was similarly cultured and the results were compared. The incidence of colony formation in normal persons approximated the number found in normal areas of the patients with nummular eczema. There was, however, a marked increase in the number of colonies found in the eczematoid plaques. Patients with allergic eczematous contact dermatitis studied by this technique during the first few days of their reaction failed to show an increased staphylococci colony count. The authors suggest that medications effective against staphylococci, such as iodochlorhydroxyquin (Vioform) tars and antibiotics, are indicated in the treatment of nummular eczema. They conclude that "nummular eczema, as a disease entity, can be satisfactorily explained by the triad of etiological components, namely, (1) poor nutrition, (2) bacterial allergy to the allergens of the staphylococci, and (3) bacterial invasion of the skin by the Staphylococcus." R. W.

The Chromium Content of Cement and Its Significance in Cement Dermatitis. Denton, C. R., Keenan, R. G., and Birmingham, D. J.: J. Invest. Dermat. **23**: 189, 1954.

Samples of cement were analyzed chemically and were found to contain chromium. Of the total chromium present, only a small portion was water-soluble. Hexavalent chromium accounted for over one-half of the water-soluble chromium.

A patient, strongly sensitive to potassium dichromate, was patch tested with the filtrates of several cement samples. The concentration of hexavalent chromium in these filtrates was less than 0.0004 per cent in terms of potassium dichromate. Positive reactions to patch tests with these filtrates were obtained on repeated testings. These findings seemed to indicate that cement contains soluble chromium in sufficient concentration to induce and maintain an allergic contact type dermatitis in a susceptible individual. M. C.

Miscellaneous Allergies

Analysis and Standardization of House Dust by Gel Diffusion. Wodehouse, R. P.: Ann. Allergy **12**: 363, 1954.

The gel diffusion technique is offered as a method of standardizing dust extract. It was determined that dust extracts contain at least three different antigens which give precipitating bands with antibodies of their homologous antisera or with sera prepared with other dust extracts. One of the three

precipitation bands is usually more prominent than the others and is considered to represent the major dust antigen, while the others represent minor antigens. Although all the minor antigens may or may not be present in any single dust extract, the major antigen is common to them all. Dust extracts prepared from materials obtained from a single source have the same antigens in nearly similar proportions. Dusts from diverse sources may contain the same antigens, but these occur in very different proportions. Pooled antidust rabbit serum may be used to standardize the dust extracts and after such standardization may be lyophilized and used as a means for standardizing other dust extracts. This is accomplished by the use of a graph in which the rate of penetration of the precipitating bands is plotted against the logarithm of the concentrations of the extract. F.

Rectal Use of Ergotamine Tartrate and Caffeine Alkaloid for the Relief of Migraine. Graham, J. R.: New England J. Med. **250**: 936, 1954.

Rectal suppositories of ergotamine tartrate and caffeine alkaloid were used in the treatment of 577 attacks of migraine occurring among 100 patients. Results were considered good where the patient experienced complete relief of headache within three hours after the medication was administered and fair when complete relief was obtained within three to six hours. The results were good in 73 per cent of the trials, fair in 17 per cent, and poor in 10 per cent. Unpleasant side effects were reported in only 5 per cent of the trials. E. W.

Acute Pericarditis Associated With Serum Sickness. Goldman, M. J., and Lau, F. Y. K.: New England J. Med. **250**: 278, 1954.

Two cases of acute pericarditis associated with serum sickness are reported. The first patient, a 15-year-old boy, developed serum sickness after the administration of tetanus antitoxin. In addition to the usual signs, physical examination revealed an increased area of cardiac dullness and a loud pericardial friction rub. Complete recovery occurred in two weeks. Laboratory data were not mentioned. The second patient, a 35-year-old Negro, developed serum sickness one week following the administration of tetanus antitoxin. He showed all the signs of serum sickness and, in addition, a loud pericardial rub was heard. This sound changed in intensity through the respiratory cycle, but persisted, even when the breath was held. The rub persisted for twenty-five hours. Five roentgenograms of the chest taken during the course of the illness were reported as normal. An electrocardiogram on admission revealed inverted T waves in leads aVL, aVF, V_3 to V_6, findings consistent with pericarditis. After treatment with cortisone, an electrocardiogram revealed normal T waves. When cortisone therapy was discontinued, the electrocardiogram showed T waves of low amplitude to inverted. Some time later, these electrocardiograms again showed a normal pattern. E. W.

Anaphylaxis

Increased Susceptibility of Mice to Anaphylactic Shock Following Cobalt-60 Gamma Radiation. Stoner, R. D., and Hale, Wm. M.: J. Immunol. **72**: 419, 1954.

Young mice were injected subcutaneously with a single dose of alum-precipitated tetanus toxoid and were then irradiated with sublethal doses of cobalt-60 gamma radiation. At varying intervals thereafter, normal and irradiated mice were challenged by the intravenous administration of fluid tetanus toxoid.

An increased susceptibility to anaphylactic shock in the radiated mice developed two days following radiation. This reached a maximum at seven days, when 100 per cent of the irradiated mice succumbed after challenge with the antigen, whereas 82 per cent of the control animals survived.

Several antihistaminic agents afforded almost complete protection from fatal anaphylaxis in irradiated mice. However, no significant difference in sensitivity to histamine given intravenously was found between irradiated and nonirradiated mice.

It was suggested that the enhancing effect of gamma irradiation upon the severity of the anaphylactic response in mice was not due to an increased sensitivity to histamine. The protective action of the antihistaminics was not explained. M. C.

The Effect of Biologic and Chemical Agents on the Experimental Production of Arteritis by Passive Sensitization. II. Nitrogen Mustard. Cohen, S. G., Walsh, J. W., and Dzury, D. S.: J. Immunol. **73**: 100, 1954.

Rabbits were given nitrogen mustard for one to two weeks in sufficient doses to induce and maintain a leukopenia. These and normal rabbits were passively sensitized with rabbit antihorse serum and challenged one-half hour later by the intravenous administration of horse serum. The animals were sacrificed twenty-four hours after challenge and sections of their lungs were studied histologically. "Typical lesions of panarteritis and periarterial infiltration of eosinophiles, lymphocytes and polymorphonuclear leukocytes, and eosinophilic infiltration into the media and intima of the small pulmonary arteries and pulmonary arterioles" were found with almost equal frequency among treated and nontreated animals.

These results indicated that the suppressive effect of nitrogen mustard on arterial lesions due to hypersensitization mechanisms could not be attributed to "an interference with in vivo antigen-antibody reactions." Neither could this suppressive effect be attributed to "an alteration of the tissue response to antigen-antibody combinations by an anti-inflammatory action or through a deficiency of reacting cells secondary to the induced leukopenia." The inhibition of antibody formation was considered a more likely explanation for the suppressive action of nitrogen mustard on the development of vascular lesions of hypersensitivity seen in active sensitization of rabbits. M. C.

Inhibition of Antibody Formation in Mature Rabbits by Contact With the Antigen at an Early Age. Hanan, R., and Oyama, J.: J. Immunol. **73**: 49, 1954.

Pregnant rabbits received intravenous injections of alum-precipitated bovine serum albumin (BSA). Following delivery, the litters were injected at regular intervals with BSA for as long as eight months. Some animals received a mixture of BSA and egg albumin later in the experiment. Blood samples taken at intervals were tested for the presence of precipitins or for their ability to induce passive anaphylaxis in guinea pigs.

Rabbits subjected to early immunization with BSA did not develop antibody to this antigen with the initial immunization or at a later period when the animals were more mature. Formation of antibody to egg albumin, an unrelated antigen which was mixed with BSA, was also inhibited in these animals. Prenatal immunization alone failed to produce this effect.

It was suggested that the presence of antigen in the formative stage of an organism might give rise to some mechanism for disposing of the antigen other than by antibody formation. M. C.

Production of Lipemia-Clearing Factor During Anaphylactoid Shock. Havel, R. J., and Boyle, E.: Proc. Soc. Exper. Biol. & Med. **85**: 468, 1954.

Dogs were shocked by the intravenous injection of peptone or other histamine-liberating compounds. In some instances protamine sulfate, an antiheparin agent, was injected one hour later. The animals were bled at intervals and the clotting time and lipemia-clearing factor (CF) were measured. Determinations of the latter factor were made by incubating plasma with a lipemic substrate and noting the change in optical density of the mixture.

Significant CF activity was present in the plasma of every dog who went into shock. CF activity was usually maximal thirty minutes or more after shock occurred. In most instances, there was an associated increase in clotting time. When protamine sulfate was given following shock, CF activity was abolished. Since heparin prolongs clotting time, increases CF activity, and is inactivated in the presence of protamine sulfate, it seemed likely that an endogenous heparinemia had been produced during anaphylactoid shock in dogs. M. C.

An Unidentified Antibody in Anti-egg Albumin Sera Revealed by the Agar Diffusion Technic. Methods For Its Immunochemical Analysis. Vaughan, J. H., and Kabat, E. A.: J. Immunol. **73**: 205, 1954.

Rabbits were injected intravenously with purified antigens prepared from egg white and were bled at intervals thereafter. The sera were analyzed for specific antibody by the quantitative precipitin technique and for traces of antibody to impurity by a special technique devised by the authors. A previously unidentified antibody in anti-egg albumin sera was found. This antibody, designated anti-EW_x, gave a characteristic precipitin curve. The specific antigen, EW_x, was estimated to constitute less than 1 per cent of the total protein of egg white. The antibody was found in anti-egg white sera but not in anticonalbumin sera. The importance of such trace constituents in antigens used for purposes of immunization was stressed. M. C.

Pharmacology, Physiology, and Pathology

Antagonism of Cortisone to Body Temperature-Reducing Effect of Histamine. Kind, L. S.: Proc. Soc. Exper. Biol. & Med. **85**: 371, 1954.

Pertussis-inoculated and untreated mice were placed in a thermostatically controlled room at 18° C. Rectal temperatures of all animals were taken by means of a thermocouple. The animals were given subcutaneous injections of histamine and the average temperature of survivors at various time intervals after histamine administration was recorded. A similar experiment was performed in which the animals had been treated with cortisone for eighteen hours prior to receiving histamine.

Pertussis-inoculated mice were more sensitive to the temperature-reducing effect of histamine than untreated animals. At two hours after the injection of histamine, the inoculated group had an average temperature fall of approximately 8 degrees as compared to a fall of 2 degrees in the control group. Cortisone reduced the fall in body temperature after histamine in both groups.

The temperature-reducing effect of histamine in mice was offered as a convenient method to study cortisone-histamine antagonism. M. C.

Changes in Patterns of Secretion of Corticosteroids in Rabbits After Prolonged Treatment With ACTH. Kass, E. H., Hechter, O., Macchi, I. A., and Mou, T. W.: Proc. Soc. Exper. Biol. & Med. **85**: 583, 1954.

Rabbits were injected daily with ACTH for varying periods of time, following which adrenal vein blood determinations were made for corticosteroids. The adrenal vein blood was collected from a segment of the vena cava so isolated that only left adrenal vein blood could enter it. To obtain sufficient corticosteroid for analysis, adrenal vein bloods from identically treated rabbits were pooled and analyzed as a single sample.

The adrenal vein bloods from untreated rabbits or those receiving one injection of ACTH contained corticosterone but no measurable hydrocortisone. When ACTH was given for one week, hydrocortisone and corticosterone were both found in the adrenal vein blood in a ratio of 1:2. When the administration of ACTH was continued for three or four weeks, hydrocortisone predominated over cortisone in the adrenal secretion in the ratio of 4:1.

Therefore, the prolonged administration of ACTH in the rabbit led to an alteration in the pattern of secretion of corticosteroid, so that hydrocortisone became the predominant steroid component of adrenal vein blood. This was considered evidence against the concept that the adrenal secretions of different species of animals are fixed. The mechanisms involved in the changes produced by prolonged administration of ACTH are discussed.

M. C.

Autoradiographical Distribution and Excretion Studies With S^{35}-Labeled, Penicillin. Ullberg, S.: Proc. Soc. Exper. Biol. & Med. **85**: 550, 1954.

Radioactive (S^{35}-labeled) crystalline sodium penicillin was injected intravenously into mice, which were killed and frozen at different intervals after injection. The frozen mice were sectioned and the distribution of penicillin in the various tissues of the body was studied by autoradiographic techniques.

The concentration of penicillin in the lungs approximated that of the blood. In the kidneys the concentration of penicillin was always higher and in the liver it was usually higher than in the blood. In most other tissues, it was considerably lower. These results correlated well with those obtained with standard methods of microbiologic assay for penicillin. M. C.

Effect of Epinephrine on Thyroid Hormone Level in Blood. Eskelson, C. D., Firschein, H. E., and Jensen, H.: Proc. Soc. Exper. Biol. & Med. **85**: 637, 1954.

Rats were injected intraperitoneally with thyrotrophin (TSH), epinephrine, and thyroxin, either alone or in various combinations. Eighteen hours before sacrifice, each animal was injected with I^{131} and the organic-bound I^{131} content in the serum was measured after the animal was killed.

The organic-bound I^{131} in blood was lowered by the administration of epinephrine. This response occurred when epinephrine was administered alone, or in combination with either TSH or thyroxin and was attributed to an increased utilization of circulating thyroid hormone caused by epinephrine.

It was suggested that the estimation of the blood organic I^{131} concentration was inadequate in itself as a test of thyroid function, since this test merely reflected the amount of circulating thyroid hormone at a particular time period. M. C.

Plasma Volume Changes in Egg White-Injected Rats. Effect of Cortisone. Williams, F.: Proc. Soc. Exper. Biol. & Med. **86**: 77, 1954.

Rats were injected intraperitoneally with egg white, and at varying intervals thereafter plasma volume determinations were made by the Evans blue technique. A decrease in plasma volume began about one half-hour after injection, reached its lowest value about one and one-half hours later, and returned to normal by the fifth hour. Cutaneous edema, which developed in all these animals, closely paralleled the changes in blood volume.

Similar experiments were performed on adrenalectomized rats and on cortisone-treated rats. In the former group, not only did the egg white injection cause a greater loss of plasma than occurred in intact animals, but edema and irreversible shock developed within one hour. In animals pretreated with cortisone, the loss of plasma was significantly less than in unprotected animals.

Direct microscopic observations of small blood vessels of these animals were made during the experiments. Intact rats showed no marked circulatory changes until about one and one-half hours after injection, at which time blood flow was slowed down in the dilated and hyperemic arterioles and capillaries. Some clumping of blood cells occurred in the venules. These changes occurred earlier and were more severe in adrenalectomized animals, while cortisone-pretreated animals developed no disturbances in capillary circulation. It was suggested that cortisone may act by preserving capillary function and maintaining plasma volume above the critical level. M. C.

An Hypothesis Concerning the Pathogenesis of Systemic Lupus Erythematosus. Gold, S. C.: Brit. J. Dermat. **65**: 43, 1953.

The difference between localized and systemic types of lupus erythematosus is purely clinical, since no biochemical, hematologic, or histologic tests have been found to differentiate between them. It is suggested that the localized cutaneous disease is a manifestation of sensitivity to an infective focus. The following hematologic abnormalities may be characteristic of the systemic cases: anemia, leukopenia, depression of platelets, false positive Wassermann and Kahn reactions, the ability of the patient to form multiple antibodies to transfused blood, the ability of serum from these patients to agglutinate sheep cells distinct from heterophil antibody, fibrinolysis on incubation of clotted blood often complete at 37° C., hyperglobulinemia with reversal of the normal albumin/globulin ratio, the presence of the L. E. cell, a positive Coombs test, and occasionally an increase in cold agglutinins. It is suggested that the disseminated type of disease represents a state of hyperimmunity with the formation of useless antibodies and autoantibodies. This state arises through lack of adequate restraint normally supplied by the pituitary-adrenal axis, an event which occurs more frequently in the young adult female in whom the pituitary-adrenal system has to maintain a regular state of hormonal flux and may be more readily upset. E. W.

Studies on Local Antibody Production. Demonstration of Agglutination By Lymphocytes. Hayes, S. P., and Dougherty, T. F.: J. Immunol. **73**: 95, 1954.

Mice were inoculated with capillary tube depots containing bacterial antigens, horse serum, or saline. The animals were sacrificed four to six days later and loose connective tissue spreads were prepared from the inoculated areas. A dilute suspension of homologous bacterial antigen was added to the tissue spread, which was then incubated from one to two hours. The preparations were then stained and examined microscopically.

Lymphocytes in the loose connective tissue spreads which had been in contact with bacterial antigen depots were surrounded by parallel rows of agglutinated homologous bacteria. This phenomenon was not observed in tissue spreads prepared from mice inoculated with saline or horse serum depots. It was concluded that the lymphocytes were responsible for the phenomenon of surface agglutination. These experiments provided additional evidence that lymphocytes are specifically associated with the process of local antibody formation. M. C.

Quantitative Serological Determinations of Antibody Formation in X-Irradiated Rabbits. Silverman, M. S., and Chin, P. H.: J. Immunol. **73**: 120, 1954.

Rabbits were exposed to a sublethal dose of whole-body irradiation and, after twenty-four hours, were injected with crystalline egg albumin mixed with Freund's adjuvant. Nonirradiated rabbits served as controls. After immunization, the animals were bled at intervals and their sera were titrated for precipitable antibody nitrogen. The primary antibody response of the x-irradiated rabbits was inhibited. Even twenty-seven weeks after irradiation when presumably they had recovered from radiation injury, the immunologic response of irradiated animals never equalled that of the controls. However, whole-body irradiation had no effect on the anamnestic reaction. M. C.

Antibody Formation and the Effect of X-Radiation on Circulating Antibody Levels in the Hypophysectomized Rat. Nagareda, C. S.: J. Immunol. **73**: 88, 1954.

Hypophysectomized rats were injected intravenously with a suspension of sheep erythrocytes, and the antisheep erythrocyte hemolysin titers in their sera were measured from four to twelve days later. Similar experiments were done on hypophysectomized rats that had been exposed to a single dose of total-body x-radiation of 500 r twenty-four hours prior to immunization. In some x-irradiated animals the spleens were shielded by lead.

Hypophysectomy per se did not alter the antibody response of the rat to sheep erythrocytes. Although a marked inhibition of antibody formation occurred in the x-irradiated rats, the spleen-shielded irradiated animals retained their capacity to produce high hemolysin titers. M. C.

The Effect of Cortisone and Adrenocorticotropic Hormone on Passively Transferred Delayed Hypersensitivity to 2,4-Dinitrochlorobenzene in Guinea Pigs. Seebohm, P. M., Tremaine, M. M., and Jeter, W. S.: J. Immunol. **73**: 44, 1954.

Guinea pigs were actively sensitized by the repeated cutaneous application of 2,4-dinitrochlorobenzene. After sensitization, sterile mineral oil was injected intraperitoneally into each animal to evoke an exudate. A suspension of exudate cells was obtained and injected intra-abdominally into white guinea pigs. These animals were skin tested with 2,4-dinitrochlorobenzene forty-eight hours later. In some experiments, some of the donor and recipient animals were given cortisone or ACTH.

Normal guinea pigs became passively sensitized to 2,4-dinitrochlorobenzene following the intraperitoneal injection of exudate cells from actively sensitized animals. This transfer was not prevented when the donor animals were treated with ACTH or cortisone, even though the exudative reaction to the intraperitoneally injected mineral oid was partially suppressed in those animals.

Recipient animals treated with ACTH prior to passive sensitization showed sharply diminished passive transfer reactions. These reactions were not diminished in cortisone-treated recipients. Because of this difference, it was suggested that the adrenal-stimulating effect of ACTH produced a hormone different from cortisone. M. C.

A Study of the Blocking Effect of Plasma and of Lysed Red Blood Cells on Delayed Allergic Reactions. Rostenberg, A., Jr., and Brebis, G. J.: J. Invest. Dermat. **23**: 3, 1954.

Patients with sarcoidosis, Hodgkin's disease, and papulonecrotic tuberculides were bled, and preparations of their plasma and lysed red blood cells were obtained. Recipients were selected who gave moderate positive delayed skin reactions to tuberculin and trichophytin. These subjects were then tested with a mixture of antigen and either the plasma or the lysed red blood cells of the donor. The antigen was made up in various dilutions. When no delayed skin reaction occurred to a test with a mixture containing a concentration of allergen which previously had produced a definite positive reaction in one-half that strength, a block was considered to have occurred.

Of the eighty-two tests performed, blocking was achieved in twenty-one of them. Lysed red blood cells produced blocking thirteen times and plasma eight times. The blocking effect was not obtained constantly with any one blood and varied with the recipients tested and with the allergen. Only the tuberculin reaction was blocked in some recipients and only the trichophytin reaction in others.

The blood of sarcoid patients seemed to have a more pronounced blocking ability than blood from nonsarcoid patients. It was suggested that the blood of sarcoid patients might contain a substance, usually labeled an anticutin, which combined with the antigen in vivo and neutralized its allergenic properties. M. C.

Studies on the Transfer of Lymph Node Cells. IV. Effects of X-Irradiation of Recipient Rabbits on the Appearance of Antibody After Cell Transfer. Harris, T. N., Harris, S., Beale, H. D., and Smith, J. J.: J. Exper. Med. **100**: 289, 1954.

The popliteal lymph nodes were removed from rabbits that had been injected in the hind foot pad with a killed suspension of dysentery bacilli three days earlier. A cell suspension of these lymph nodes was injected intravenously into normal recipient rabbits that had been subjected twenty-four hours earlier to doses of irradiation sufficient to suppress their antibody formation response. One-half the irradiated animals died within a two-week period. On the first day after transfer agglutinins were found in the recipient rabbit sera, in both irradiated and nonirradiated animals, but higher titers were consistently obtained in the irradiated group. The titer remained as high on the sixth or seventh day as on the third day in most of the irradiated animals, but in normal recipients the titer declined after the third or fourth day.

Whole-body irradiation was applied to the recipient animal one hour after the transfer of lymph node cells (removed from the donor three days after antigen injection). Serum titers of antibody in the recipient were reduced markedly by this procedure. When irradiation was carried out one day after the reception of the cell suspension, antibody titers were diminished slightly as compared with controls. Irradiation performed after a two-day interval failed to affect the resulting titer. It is suggested that irradiation

damage to the recipient animal's defense mechanisms, including his phagocytic capabilities, might have a sparing effect on the injected cellular elements and thus account for the higher titers of antibody observed in the pre-irradiated animals. K.

The Relation of Allergy Reagins to Electrophoretic Components of Serum. Campbell, D. H., Cann, J. R., Friedman, T. B., and Brown, R.: Science **119**: 289, 1954.

The sera of seven untreated patients which contained circulating skin-sensitizing antibodies were fractionated by the electrophoresis-convection method. All serum fractions were tested for their specific affinity for ovalbumin by means of a special precipitin test. The fractions in several dilutions were injected intracutaneously into normal persons in 0.1 ml. amounts and forty-eight hours later these sites were tested intracutaneously with antigen.

Although in most instances it was not possible to determine conclusively which serum components contained reaginic activity, it became evident that reagins were not characteristically associated with the gamma-globulin component of these sera. In a ragweed-sensitive patient, activity appeared to reside in the alpha$_2$ component. This preparation contained some material that combined with ovalbumin, although there was no clinical history of egg sensitivity in the donor.

All serum fractions of one patient with clinical egg sensitivity failed to combine with ovalbumin. This patient proved to be sensitive only to ovomucin.

The discrepancies between reaginic titers and serum component concentrations could not be explained on the basis of the possible presence of "neutralizing" antibodies in the sera, since all sera came from persons without prior treatment. M. C.

Eosinophilic Granuloma of the Lungs. Mazzitello, W. F.: New England J. Med. **250**: 804, 1954.

Two cases of eosinophilic granuloma of the lung in young male patients are reported. The diagnosis in each case was made by thoracotomy and lung biopsy. In both cases the lesions were apparently limited to the lungs, which were extensively involved. Neither blood nor sputum eosinophilia was found. Treatment with ACTH and cortisone was followed in each case by some improvement. A review of the literature is included. E. W.

Miscellaneous

Eosinophils of Blood During Prolonged Exposure to Cold and Chronic Administration of Cortisone Acetate. Denison, M. E., and Zarrow, M. X.: Proc. Soc. Exper. Biol. & Med. **85**: 433, 1954.

The level of circulating eosinophils was measured in rats, which were exposed to a low environmental temperature (2 ± 2° C.) for a period of ninety days, and in rats treated with cortisone for twenty-one days. Within six hours after exposure to cold, a fall of 86 per cent in the eosinophils of the blood occurred. However, the eosinophil count returned to normal at twenty-four hours despite continued exposure to cold. During the remainder of the period of cold exposure, the level of eosinophils remained similar to or greater than the pre-exposure volume, except for a temporary drop on the fifteenth day. In cortisone-treated rats, it was possible to maintain a constant depressed level of circulating eosinophils when sufficient hormone was given daily.

The initial fall in circulating eosinophils in rats exposed to cold was attributed to an outpouring of adrenal corticoids in response to increased stress. The effect of increased amounts of adrenal corticoids was soon counteracted by the increasing needs of the organism. Hence, as the animal became adapted to the cold environment, a eucorticoid state developed with return of the eosinophil level toward normal. M. C.

The Antigenic Composition of Ammodytes Viper Venom. Piantanida, M., and Muic, N.: J. Immunol. **73**: 115, 1954.

The protein fractions, the water-soluble fraction, and the whole substance of pooled Ammodytes snake venom were analyzed for antigenic activity by means of the Oudin test and paper stain chromatography. The lethal effects of whole venom on mice were found to reside in the water-soluble fraction and consisted primarily of a rapidly acting neurotoxin which paralyzed the respiratory center. There was present also a second toxic substance which produced pulmonary hemorrhage. No antigenic properties were found in this water-soluble fraction.

The precipitated protein fractions consisted of three antigenic components. These fractions had significant hemorrhagic activity but only moderate neurotoxic activity. Since venom antiserum has a pronounced protective effect against all toxic manifestations of venom, it was postulated that the nonantigenic components in whole venom are conjugated to the antigenic proteins. It was supposed that a disassociation of these principles had occurred in these experiments. M. C.

Cortisone and ACTH in Pregnancy. Katzenstein, L., and Morris, A. J.: New England J. Med. **250**: 366, 1954.

A case of dermatitis herpetiformis occurring during pregnancy in a 36-year-old patient is reported. During the last five months of pregnancy, this patient received approximately 3.0 Gm. cortisone and 1.3 Gm. of ACTH. She delivered a normal male infant whose subsequent growth and development were normal. Despite contradictory experimental evidence, the few clinical cases that have been reported suggest that steroid therapy during pregnancy results in no apparent damage to the infant. E. W.

Treatment of Allergic Conditions With Sustained Release Chlorprophenpyridamine Maleate. Rogers, H. L.: Ann. Allergy **12**: 266, 1954.

Thirty patients were treated with sustained release capsules of chlorprophenpyridamine maleate (Teldrin Spansule). The average dose in adults and older children was a single 12 mg. capsule daily. There was one 4-year-old child in the series who was given 8 mg. per day. Eleven patients obtained "excellent" relief; five "very good"; nine, "good"; two, "slight"; and three, "no" relief. Side effects were noted in three patients and consisted of bladder irritation, sleepiness, and reddening of the skin. The results obtained with the sustained release capsule were superior to those obtained with ordinary tablets of the same drug. F.